34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

Computational Basis for Risk Stratification of Peripheral Neuropathy from Thermal Imaging

E. Simon Barriga*,†, Viktor Chekh††, Cesar Carranza†, Mark R. Burge†††, Ana Edwards*, Elizabeth McGrew*, Gilberto Zamora*, and Peter Soliz*

*VisionQuest Biomedical LLC, Albuquerque, New Mexico 87106
†Electrical and Computer Engineering Department, University of New Mexico, Albuquerque, New Mexico 87131
††Computer Science Department, University of New Mexico, Albuquerque, New Mexico 87131
†††Clinical and Translational Science Center, University of New Mexico, Albuquerque, New Mexico 87131
Email: sbarriga@visionquest-bio.com

Abstract*— The goal of this paper is to present a computer-based system for analyzing thermal images in the detection of preclinical stages of peripheral neuropathy (PN) or diabetic foot. Today, vibration perception threshold (VPT) and sensory tests with a monofilament are used as simple, noninvasive methods for identifying patients who have lost sensation in their feet. These tests are qualitative and are ineffective in stratifying risk for PN in a diabetic patient. In our system a cold stimulus applied to the foot causes a thermoregulatory and corresponding microcirculation response of the foot. A thermal video monitors the recovery of the microcirculation in the foot plantar. Thermal videos for 8 age-matched subjects were analyzed. Six sites were tracked and an average thermal emittance calculated. Characteristics of the recovery curve were extracted using coefficients from an exponential curve fitting process and compared among subjects. The magnitude of the recovery was significantly different for the two classes of subjects. Our system shows evidence of differences between both groups, which could lead to a quantitative test to screen and diagnose peripheral neuropathy.

Peripheral Neuropathy; Thermal Imaging; Diabetes.

I. INTRODUCTION

According to the CDC, diabetes afflicts an estimated 171 million people worldwide, including more than 24 million Americans [1]. Diabetic patients are at risk for a wide array of complications including heart disease, kidney disease (nephropathy), ocular diseases (diabetic retinopathy), and peripheral neuropathy (diabetic foot) [2]. It is estimated that 50% of diabetics have some degree of neuropathy. Fifteen percent, or two million, of these will develop a foot ulcer during their lifetime [3]. Foot ulcers are the main cause (85%) of lower extremity amputation in patients with diabetes [4].

Neuropathy causes the impairment of blood flow in the diabetic foot [5]. Patients with long-standing neuropathy will have poor thermoregulation and hence altered blood flow and cutaneous microcirculatory dysfunction [6].

Monofilament testing is a common, noninvasive method for identifying patients who have lost sensation in their feet. The Semmes-Weinstein nylon mono-filaments are used for light touch assessment. A series of increasingly thick filaments are tested. The inability to feel the 10 gm filament indicates that patient is at risk for advanced stages of peripheral neuropathy, *i.e.* foot ulceration. Data in support of location of insensate sites for determining risk and prediction onset of peripheral neuropathy have been reported as subjective and lacking quantitative indication [7].

The objective of this research is to show that differences in the functional signals as measured by a thermal imaging device could reveal pre-clinical indications of peripheral neuropathy. In this paper we describe the protocol for preparing the subject by applying a cold pressor stimulus to the foot, the thermal imaging sequence for collecting the recovery signal, the frame-to-frame registration of the thermal video, the feature extraction of the recovery signal, and the results from performing this test on 8 subjects divided into three groups: Normal controls, patients with diabetes but no PN, and patients with PN.

II. METHODOLOGY

A. Medical Thermography

Dynamic infrared thermometry studies have previously been performed in patients with hand-arm vibration syndrome (HAVS) [8]. Results of those studies showed significant differences between HAVS patients and controls in terms of baseline temperature, rewarming time and rate of recovery after cold provocation of patients' hands. Although thermal imaging has been used previously for structural imaging of the diabetic foot [9], those studies have focused only on discovering a difference in absolute skin/tissue temperature differences and non-dynamic spatial variations. Our dynamic, functional imaging technique is different and avoids the short comings of static thermal measurements by applying a thermal stimulus which will produce a response in the capillary bed. The effect of cooling the foot's capillaries to 10 to 15° C below the core body temperature of 37° C is easily detected with a thermal imaging device. Visually, one can see the changes in appearance due primarily to changes in blood flow, i.e. thermal auto-regulation. The time to recover back to its normal state is the signal that we are measuring to detect pre-clinical stages of peripheral neuropathy.

B. Digital Functional imaging device

The thermal functional imaging apparatus consists of a thermal imaging device, the FLIR Model SC 305 infrared camera, which acquires a thermal radiant emittance video from the scene or object. The FLIR imager operates in the 7.5 to 13 μm region of the infrared spectrum.

At these wavelengths, one is measuring the thermal emission from the field of view, in our case the plantar region of the subject's foot. The FLIR thermal camera comes with a data acquisition system that operates at 8.6 frames per second. The video format is 320 pixels by 240 pixels, 14 bits per pixel. It has high-thermal-sensitivity (less than 0.05° C) and is a portable device, e.g., does not require liquid nitrogen cooling. During the fifteen minute thermal imaging sequence 7,740 frames of thermal images are collected.

C. Imaging protocol

The imaging protocol begins with cleaning the feet after socks have been removed, followed by application of reflective markers and an initial surface temperature reading taken with a hand-held IR thermometer (American Scientific Resources, Model 11-900) at the regions of interest of both feet (ROI as seen in Figure 1). These six points were selected based on the accepted test points in a clinical diabetic foot exam. Feet are imaged for two minutes with the FLIR thermal infrared cameras to record the baseline thermal signal. Only one foot (experimental) is exposed to the cold provocation at any one time. Covered by a thin waterproof plastic bag, the experimental foot remains dry when subjected to the cold pressor test through immersion in cool water (13° C – 14°C) for 5 minutes. After removal from the water, temperature readings are recorded again with the hand-held thermometer at each of the ROIs.

The next phase is the recovery stage, where fifteen minutes of simultaneous thermal IR and spectral video imaging of both feet is recorded. Temperatures with the hand-held thermometer are collected at the end of the fifteen minute-recording period.

Figure 1. Subject's right foot and measurement ROIs.

D. Data Description

In this paper we present data collected from eight subjects. Of them, three are normal controls, three are diabetics who have not been diagnosed with peripheral neuropathy, and two are patients with diagnosed peripheral neuropathy. The subjects have been grouped into three age-matched brackets for analysis, as age can be a factor in thermal response differences of the cooled foot. A 15 minute thermal video was recorded for each subject. Temperatures were also recorded with a standard infrared thermometer.

E. Motion Tracking of Thermal Features

In order to determine the recovery rate for each region of interest (ROI) on the foot, an accurate tracking algorithm must be applied.

The motion tracking starts with the demarcation of features on the foot plantar. Silver foil self-adhesive fiducial marks were placed at the six locations of the foot to help with precise automatic tracking of the foot. The ROIs selected are typical areas where the monofilament test is commonly performed. The ROIs are illustrated in Figure 1.

We preformed the automatic ROI tracking using Matlab. For this, we select two reference areas, one at the top and one at the bottom of the foot, and track their positions using normalized cross-correlation between the first frame and the current video frame. Once the new position of the reference areas is calculated, we calculate the new location of each ROI using a geometrical transformation.

The tracked videos are then used to extract the IR values of the six ROIs. We use different sizes of ROIs for different markers. For the big toe, a region of 8-by-8 pixels is used, for the middle toe we use a 5-by-5 pixels ROI, and for the remaining points a 10-by-10 pixels ROI is used.

For each of the six ROIs, an average radiant emittance was plotted as a function of time. A percent change was used as the metric for comparison. This change was calculated based on the minimum radiative emittance at the end of the cold application to the foot plantar.

F. Exponential Curve Fitting

The hypothesis of the thermal recovery after cold provocation is that the foot recovers its temperature proportionally to an exponential function of time. Thus, we used a curve fitting algorithm to determine the parameters for recovery of each ROI in each subject.

We fit the IR values to the model $y = A\left(1 - e^{-\lambda t}\right)$, where y is the IR value for each time point, A is the percentage of total recovery, and λ is the rate of recovery. We use an unconstrained nonlinear optimization approach to this curve fit by minimizing the sum of squares of errors between the data and the exponential function $y = A\left(1 - e^{-\lambda t}\right)$ for varying parameters A and λ. Once the curve fitting is performed, we calculated the goodness of fit parameter R^2 to assess how well each of the ROIs followed the theoretical exponential temperature recovery function.

III. Results & Discussion

A. Case 1: Neuropathy Subject

In this section we illustrate the nature of the data collected by giving a description of the findings from two subjects. This will give the reader insight into the specifics of the thermal recordings used to characterize the recovery rates for the two categories of subjects (normal controls and diabetics). In one of these experiments, the neuropathic subject is a male (age 68) with diagnosed Type II Diabetes

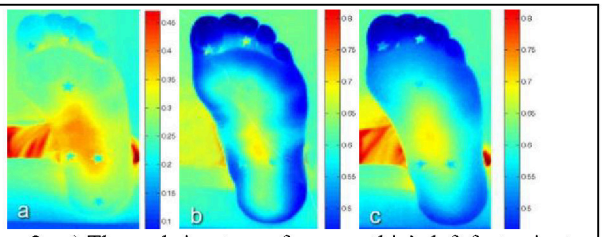


Figure 2 - a) Thermal signature of neuropathic's left foot prior to cold provocation. b) Thermal signature of subject's left foot after cold bath. c) Thermal signature of subject's left foot after recovery period.

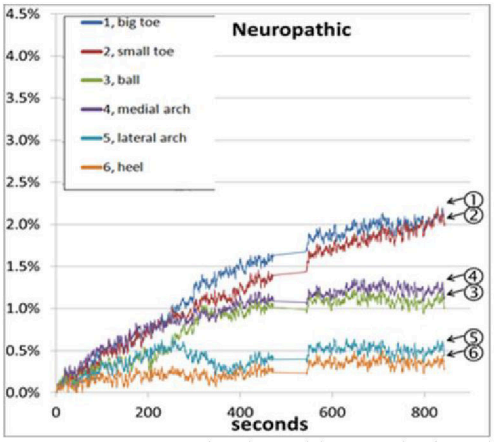


Figure 3 –recovery rates for six positions on the foot plantar for the diabetic with early, pre-clinical peripheral neuropathy.

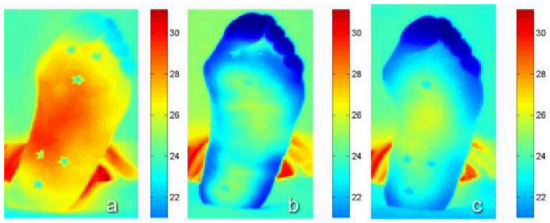


Figure 4 – a) Thermal signature of control's left foot prior to cold bath. b) Thermal signature after cold bath. c) Thermal signature after the recovery period.

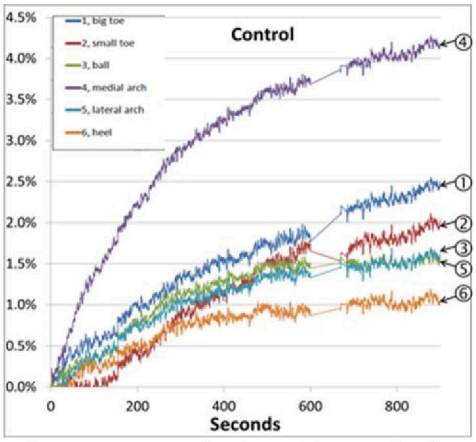


Figure 5 –recovery rates for six positions on the foot plantar for the age-matched normal.

for more than 10 years, on a prescription of insulin, with some loss of sensation on the heel suggesting possible peripheral neuropathy. In the second experiment, the age-matched control is a male (age 67).

To evaluate the microvascular function of the foot as an indicator of peripheral neuropathy and its severity, it is necessary to measure the thermal emission over a period of time and capture the recovery of the microvascular blood flow, which was inhibited by the cold provocation. This technique for measuring microvascular function was used on these two subjects.

Figure 2a gives the thermal image of the left foot for the 68-year old diabetic prior to applying the cold provocation. Figure 2b is the thermal image immediately after the left foot has been removed from the cold bath. Figure 2c is at the end of the recovery period. Darker pixels represent lower *temperatures.*

Figure 3 presents the percent change from the baseline thermal emittance for the fifteen minute recovery period. For example, the two toes (points 1 and 2) on the plot show a recovery of 2% from the starting thermal emittance magnitude. On the other extreme the heel shows only a recovery of about 0.4%.

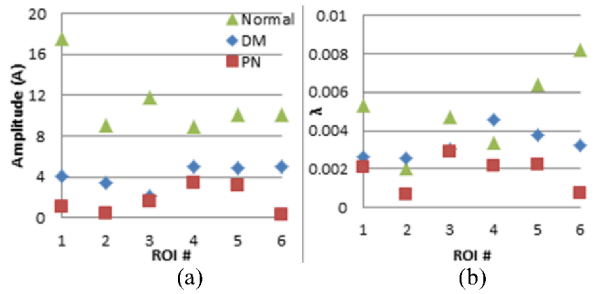
B. Case 2: Age-matched Control

Figure 4a shows the thermal image of the left foot for a 67-year old, age-matched control prior to applying the cold provocation. Figure 4b is the thermal image immediately after the left foot has been removed from the cold bath. Figure 4c is the image taken post recovery period (fifteen minutes after removal from cold bath).

The recovery traces for the control are plotted on the same scale (Fig. 5) as the neuropathic subject to show the clear difference in recovery rates. It is particularly apparent in comparison of the rate of recovery for the medial arch, where the control's recovery is 4% versus less than 1.5% for the neuropathic subject.

C. Age Controlled Group Results

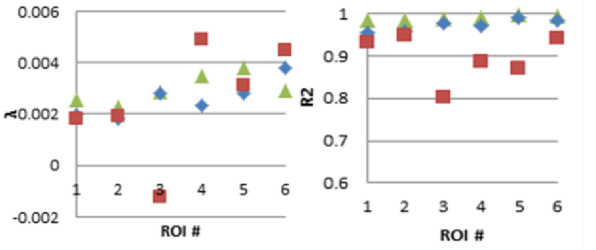
In this section we present results for two age- and gender-controlled groups of subjects that contained a triplet of normal (N), diabetic (DM), and peripheral neuropathy (PN) with ages no more than 5 years apart. For each group we calculated the values for the percent of recovery, the rate of recovery, and the R^2 goodness of fit parameter of the IR data and the fitted exponential curve. The first group consisted of three females aged 51 (N), 54 (DM), and 50 (PN). Figure 6 shows the scatter plots of the three parameters for each of the ROIs. It is evident from Figure 6a that the rate of recovery in the normal subject was higher than in the DM subject, and this in turn was higher than the PN subject. Differences are also evident in the rate of recovery coefficient (λ), which is generally higher for the normal and DM subjects (Figure 6b).



(a) (b)

Figure 6. (a) % recovery for each ROI. (b) Rate of recovery.

The second group consisted of three females aged 58 (N), 57 (DM), and 60 (PN). Figure 7 shows the scatter plots of the three parameters for each of the ROIs. In this case, the differences in the percent of recovery are evident for ROIs 3, 4, and 5 (Figure 7a. Both the N and DM subjects always have higher rate of recovery than the PN subject. However, the most important results of this group comes from the analysis of the R^2 parameter. As seen in Figure 7b, the goodness of fit of the normal subjects is close to perfect ($R^2 \sim 1$), while the DM subjects have slightly lower values for ROIs 3, 4, and 5. More relevant still, the PN subject has R^2 values in the range of 0.8 to 0.9 for those ROIs, which demonstrates that the IR recovery of this subject does not follow the expected exponential curve.



(a) (b)

Figure 7. (a) Rate of recovery. (b) Curve fit coefficient, R2.

In summary, for these experiments as many variables that might affect the thermal emission measurements have been controlled. Room temperature was controlled and recorded. The cold bath for each experiment was within 2° C. The large variation in the two sixty-year old subjects is clear evidence that there is a difference in the microvascular behavior when exposed to a cold provocation. Differences in several parameters of the age-controlled groups have also been observed in Figures 6 and 7. The differences in values for rate of recovery and goodness of fit of the data with an exponential curve can be used to create a normative range to differentiate between different stages of the disease.

IV. Conclusions

We have presented a system for quantifying changes in microvascular responses of the feet due to the presence of diabetes. Age-matched pairs of subjects have shown that, in general, the normal subjects exhibit higher percentages of temperature recovery after cold provocation than their diabetic pair. The differences in recovery are not as evident in areas of deeper tissue or fat accumulation.

The results obtained in this study are similar to the ones involving cold provocation in HAVS patients [8], where Youakim found that the HAVS patients' decrease in temperature post cold water immersion was less than the corresponding decrease in the control group. In their study the time and rate of rewarming were approximately three times faster in the control group compared to the HAVS group. These similar findings confirm that it is possible to screen patients with microvascular abnormalities using cold provocation and infrared thermography.

Future work will concentrate in creating a normative range using a large cohort of normal and diabetic subjects. This normative range can be used as a mean for quantitatively screening subjects at risk of developing peripheral neuropathy.

Acknowledgment

This work was funded by NIH grant DK 093192.

References

[1] International Diabetes Federation. Information on Global Diabetes Prevalence. In: http://www.eatlas.idf.org/Prevalence/; 2004.

[2] Boulton AJM: The diabetic foot: a global view. *Diabete Metab Res Rev* 16:S2–S5, 2000.

[3] Ramsey SD, Newton K, Blough D, McCulloch DK, Sandhu N, Reiber GE, et al. Incidence, outcomes, and cost of foot ulcers in patients with diabetes. Diabetes Care 1999; 22(3):382-7.

[4] Reiber GE, Boyko EJ, Smith DC. Lower extremity foot ulcers and amputations in diabetes. In: Harris, Cowie, Stern, Boyko EJ, Reiber GE, Bennet, editors. Diabetes in America. 2nd ed. Washington, D.C.: US Government Printing Office; 1995. p. 402-428.

[5] Rayman G, Williams S, Spencer P, Smaje L, Wise P, Tooke J. Impaired microvascular hyperaemic response to minor skin trauma in type 1 diabetes. Br Med J 1986; 292:1295-8.

[6] Cobb J, Claremont D. Noninvasive measurement techniques for monitoring of microvascular function in the diabetic foot. Int J Low Extrem Wounds 2002; 1:161-9.

[7] Miranda-Palma B, Sosenko J, Bowker J, Mizel M, Boulton A. A comparison of the monofilament with other testing modalities for foot ulcer susceptibility. Diabetes Res Clin Pract 2005;70:8-12.

[8] S. Youakim, "Infrared thermometry in the diagnosis of hand–arm vibration syndrome," Occupational Medicine 2010;60:225–230

[9] Benbow S, Chan A, Bowsher D, Williams G, Macfarlane I. "The prediction of diabetic neuropathic plantar foot ulceration by liquid-crystal contact thermography," Diabetes Care 1994; 17:835-9.